DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/5/07 has been entered.

Election/Restrictions

Applicants' election of Group I, claims 53-55, 58-63 and 67-70, drawn to an array of eukaryotic cells, i.e., plant cells in the reply filed on 6/17/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 56-57 and 72-86 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/17/08.

Status of Claims

Claims 53-63, 67-70 and 72-86 are pending.

Claims 56-57 and 72-86 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claims 53-55, 58-63 and 67-70 are under examination.

Withdrawn Rejection

In view of applicants' arguments and amendments to the claims the 35 USC 112, first paragraph (new matter) and second paragraph rejections are withdrawn. Also, the 35 USC 103 rejection over Dellaporta is withdrawn.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 53-55, 58-63 and 67-70, as amended, are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter for reasons reiterated below.

The claimed array of eukaryotic cells comprising of the properties as recited in (a)-(d) would read on a naturally occurring CHBP present in all eukaryotic cells. [The preamble, which recites "engineered to express a library of CHBP" appears

drawn to a process of manipulating a cell rather than to a positive identification of the engineered composition, CHBP. If at all the preamble is accorded, little weight, especially since it does not affect or correlate to the body of the claims.] Furthermore, an array, which is a collection of known compounds, lacks patentable utility. If it is useful as a screening tool, then perhaps a claim to a method of using the known compounds to screen or identify a novel compound contain in said array would be more appropriate to claim. The court in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion. Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential

role as an object of use-testing." *Brenner*, 148 USPQ at 696.

Response to Arguments

Applicant argues that the claimed array of eukaryotic cells is not naturally occurring because the cells are engineered to express the CHBP.

In reply, mere recitation of the term "engineered" in the preamble does not mean that it is not naturally occurring especially when the body of the claim does not recite how or what the "engineered array" comprises. The term "engineered" is not an art recognize term of the means by which a cell is produced or manipulated such that the cell is an expression cell. Please see applicants' arguments below as to the use of the art recognized term "recombinant", if this is what is intended by the term "engineered".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 53-55, 58-63 and 67-7, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with

the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record, as repeated below.

The specification fails to provide a written description of a heavy chain binding protein (CHBP) array in a eukaryotic cell wherein the CHBP polypeptide is claimed to have the recited properties of (a)-(d). There seems to be no correlation between the specific IgBP array transfected in plant cells as describe in detail in the specification i.e., the Examples and the general statements reciting the properties of the polypeptide. None of the detail description describes a CHBP array in a eukaryotic cell having the stated properties of the IgBP. It does not describe array with polynucleotides encoding protein(s) that has at least 75 % identity to a 25 consecutive amino acid portion of Ig light chain variable region and etc. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. The specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the array with the critical features of

the encoded polypeptide. The specification at e.g., page 10, lines 8-24 referred to by applicants, relates to the IgBP not in array form. Thus, no identifying characteristics or properties of the array with IgBP defined as a percent of the whole is described in the specification. No guidance or direction has been provided in the specification such that a skilled artisan would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. More importantly, the disclosure does not describe an array comprising at least 1,000 and 10,000 different binding proteins assembled by the cells in an array.

Response to Arguments

Applicant states that the Examiner has failed to consider the various actual examples in the application which describe not one but a variety of eukaryotic cell CHBP arrays. Example 1 of the application describes the cloning of heavy and light chain variable region genes from different donors of human bone marrow that contained B cells with antibodies to Clostridium difficile toxin A and B. Specification, page 44. The cDNA for the variable heavy and light chain genes is clearly polyclonal in nature because it was isolated from total bone marrow. See Specification, page 45, e.g., lines 26-30, ("The amplified regions were then ligated into a vector to encode the heavy

chain polynucleotide consisting of a signal sequence, a diversity of variable region[s] and the entire gamma constant region"). The Example describes insertion of the various heavy and light chain variable genes into a plant expression vector to produce "a recombinant population of vectors". Id. at page 46, 1st paragraph. Example 1 describes that transfection techniques were used to prepare "approximately 1,000 plants." Id. Such CHBP cell array was analyzed and found to represent a library of different CHBP. Id. at page 47, second paragraph. Example 2 describes a CHBP cell array prepared in eukaryotic (corn) cells using the heavy chain genes from Example 1 but with a hybrid constant region containing IgG and IgA sequence. Specification, page 49. Again, an array of approximately 1,000 corn plants were prepared and tested for antibodies to Clostridium difficile toxin A and B. 90 of the approximately 1,000 plants tested were determined to contain a CHBP cell with antigen binding. Id. at page 50. Example 3 of the specification describes another CHBP cell array in corn which was prepared by sexually crossing the various antigen binding plants identified in the cell array from Example 2. In addition, Example 5 describes the preparation of a CHBP eukaryotic (insect) cell array where about 8% of the cell array were determined to be antigen binding. Still further, Example 6 describes the preparation of CHBP eukaryotic

(mammalian/hamster) cell array where about 7% of the cell array were determined to be antigen binding. Applicants submit that the above demonstrates that the Specification (using the Examples alone) provides more than adequate written description for the claimed eukaryotic cell array.

IN reply, none of the Examples cited by applicants above describe the claim array of eukaryotic cells engineered to express a library of CHBP array in eukaryotic cells, comprising ….[each CHBP polynucleotide encodes] at least one CHBP polypeptide that: (a) comprises an amino acid sequence that is at **least 75% identical to a constant region tailpiece of a mu or alpha chain of a native immunoglobulin heavy chain**; (b) comprises multiple combining antigen binding sites, wherein all of the combining sites satisfy the same one of the following requirements: (i) **at least 75% identity to a 25 consecutive amino acid portion of an immunoglobulin light chain variable region; or (ii) at least 75% identity to a 25 consecutive amino acid portion of an immunoglobulin heavy chain variable region**; and (c) either (i) specifically binds to a ligand with a KD-6 moles/liter; or (ii) forms one or more covalent bonds with one or more polypeptides in the transfected cell, to generate a CHBP that specifically binds to a ligand with a KD-6 moles/liter; and (d) differs in amino acid sequence from other CHBPs in the

array; wherein the cells assemble CHBPS comprising at least four combining antigen binding sites. (Emphasis added).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 53-55, 58, 63 and 67-71, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 53 is indefinite in the recitation in paragraph(c) that either (i) specifically binds to a ligand. It is not clear whether the ligand refers to an antigen as (b) recites multiple antigen binding sites". Furthermore, (c)(ii) recites "forms one or more covalent bonds with "one or more polypeptides in the transfected cell". Does the CHBP polypeptide binds with an unknown one or more polypeptides contained in the eukaryotic cell? It is not clear whether the different terminologies use is one and the same thing.

Claim Rejections - 35 USC § 102/35 USC § 103

Claims 53-55, 58-63 and 67-71, as amended, are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over either Ma et al (Eur. J. Immunol.) or Hiatt (Nature). [This rejection is based on the interpretation that the claimed at least 75% identical to a constant region tailpiece of a mu or alpha chain of native Ig heavy chain (i.e., the full length sequence of CHBP or Ig).

Ma discloses throughout the article e.g., at page 132 under Materials and methods section including Fig. 1, the different forms of heavy chain (library as claimed) transformed in plants i.e., Plant G13, Plant G1/A and G2/A. Ma at e.g., page 133 under the RESULTS section, paragraph 3.2 discloses that 22 transgenic plants were regenerated from the transformation with light or heavy chain constructs. The antigen binding capability of the mab is disclosed at page 138, paragraph 3.4 including the figures up to page 137. Ma discloses e.g., at page 138, paragraph 3.5 the different eukaryotic cells i.e., mouse and plant cells. Ma discloses the array i.e., microtiter plates at e.g., page 7, Note 7.

Hiatt at pages 469-70 basically discloses a similar transgenic plant with antibodies. Hiatt discloses the array

i.e., the microtiter plates at e.g., page 77, col. 1, the footnote below Table 1.

The claimed properties of the polypeptides encoded by the CHBP polynucleotide are considered inherent to the CHBP polypeptide of each of Ma or Hiatt. The native Ig taught by Ma or Hiatt "engineered" to a plant cell inherently comprises (a) an amino acid sequence that is at least 75% identical to a constant region tailpiece of a mu or alpha chain of a native immunoglobulin heavy chain; (b) comprises multiple combining antigen binding sites, wherein all of the combining sites satisfy the same one of the following requirements: (i) at least 75% identity to a 25 consecutive amino acid portion of an immunoglobulin light chain variable region; or (ii) at least 75% identity to a 25 consecutive amino acid portion of an immunoglobulin heavy chain variable region; and (c) either (i) specifically binds to a ligand with a KD-6 moles/liter; or (ii) forms one or more covalent bonds with one or more polypeptides in the transfected cell, to generate a CHBP that specifically binds to a ligand with a KD-6 moles/liter; and (d) differs in amino acid sequence from other CHBPs in the array; wherein the cells assemble CHBPS comprising at least four combining antigen binding sites. [Note these properties are normally inherent to the native mab (Ig).]

Where the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same as is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. See In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972); In re Best 195 USPQ 430 (CCPA 1977).

The claimed array as well known in the art is the microtiter plates as taught by either Ma or Hiatt.

Applicants' arguments with respect to Dellaporta are moot. See the rejection above.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/T. D. Wessendorf/

Primary Examiner, Art Unit 1639